



EUROPEAN
SOCIETY FOR
PIGMENT
CELL
RESEARCH

March 1987

The **ESPCR** is born !

A foreword by Giuseppe Prota, President

Dear Members,

More than one year has passed since the European Society for Pigment Cell Research was inaugurated in Naples on the 11th December, 1985 by Natale Cascinelli, Patrick Riley and myself. I feel it is my first duty, as the President of the ESPCR, to express my thankfulness to all the people who have enthusiastically joined in this enterprise. A grateful acknowledgement should also be given to Fondazione Pro Ricerca Dermatologica (Rome), Clairol (Stamford, USA), and l'Oréal (Paris), which have provided us with the necessary funds to meet the initial costs of the establishment of the Society.

The exigency of pigment cell researchers from all Europe of having a coordinating body to give cohesiveness and organizational support to scientific

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activities gained progressive ground in the successful series of the European Workshops on Melanin Pigmentation and acquired a definite form during the last Vith EWMP in Murcia in 1985. We all should, therefore, be very grateful to the Colleagues who, over the years, have opened the doorway to this Society by excellently organizing in turn the EWMPs : J.P. Ortonne and J. Thivolet (Lyon, 1978), A.S. Breathnach (London, 1979), J. Duchon (Prague, 1981), J.A.A. Hunter (Edinburgh, 1982), C. Aubert (Marseille, 1984), J.A. Lozano (Murcia, 1985).

Although the ESPCR is still in its embryonic phase, in the very first months of its life it has infused new energy and incentives into the pigment cell community. An account of the actions taken by the Executive Council has already been given by the Secretary, Patrick Riley, in his letter of September, 1986. Here, it is just sufficient to mention the active role played by the ESPCR in promoting the restructuring of the International Pigment Cell Society currently underway and the launching of the Pigment Cell Research Journal.

Our organization is growing rapidly, we have now more than 150 active members, including several from countries outside Europe, and I feel confident that many more will join us in the near future. Such a wide participation of scientists from all countries and with a broad spectrum of interests will surely contribute to the furtherance of one of the major aims of the Society, i.e. to stimulate pigment cell research and its application to urgent human diseases. In pursuance of this and other aims of the Society, the active participation of all members is warmly encouraged, since many problems still remain to be faced and initiatives to be taken. Among these latter, a prominent place is occupied by the launching of the periodical ESPCR Bulletin, which will be edited periodically by Ferdy Lejeune in collaboration with Aodan Breathnach and Leszek Wolfram. This should not only represent a means by which news and information concerning the ESPCR activities are circulated, but, especially, should provide an open forum where new ideas are presented, the results of outstanding experiments are preliminarily communicated and controversial topics are discussed. A most significant section will be the Current Literature Compendium, where the relevant, up-to-date literature in all fields of pigment cell research will be gathered and presented in an easily accessible form. It seems superfluous to stress here the importance of this Compendium as a professional aid for a large segment of investigators and scientists. Rather, I think we all owe a word of acknowledgement to Miss Linda Albrecht (Clairol, Stamford) for her valuable assistance in the computer literature search, as well as to the Lawrence M. Gelb Research Foundation for bearing the costs of such a demanding service. I would also like to express my warmest appreciation for the active cooperation and financial contribution provided by Ferdinando Serri through the "Fondazione Pro Ricerca Dermatologica" (Roma) which allowed the editing and distribution of the Bulletin without any additional

charge for the members of the Society.

Finally, I am very pleased to announce that the first Meeting of the ESPCR will be held in Sorrento (Naples) on October 11-14, 1987. Work is underway to make this event an intellectually stimulating and socially enjoyable occasion for all members to meet and discuss problems of common interest. My colleagues and I look forward to welcoming you in Sorrento.

Giuseppe Prota
President ESPCR

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Pigment Cell Research Bulletin

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NEWS FROM THE ESPCR



THE FIRST CONGRESS

The first meeting of the Society will take place in Sorrento, Naples on October 11-14, 1987.

For details : Dr Anna Palumbo, Dept of Organic and Biological Chemistry, Via Mezzocannone 16, I - 80134 Naples, Italy.

As the previous European Workshops on Melanin Pigmentation, the format of the Meeting will be such as to provide an open forum where new information and current trends in pigment cell research can be communicated and discussed. The aim of the organizers is to be responsive to pure and applied research from both academic and industrial environments.

Scientific programme

The scientific programme will include oral communications, poster sessions and invited lectures on topics of current interest deserving special attention, such as :

- 1) the physical and chemical bases of melanin pigmentation;
- 2) enzymic and chemical control of melanogenesis;
- 3) neuromelanin and other extra-cutaneous melanins.

Research seminars will also be organized on "how to do it" aspects of new techniques and current methods of investigation in pigment cell biology.

THE EXECUTIVE COMMITTEE OF ESPCR

For the time being, the Executive Committee is the following :

President : Giuseppe Prota (Napoli)

Secretary : Patrick Riley (London)

Members : Fritz Anders (Giessen)
Natale Cascinelli (Milano)
Ferdy Lejeune (Brussels)
Jose Lozano (Murcia)
Hans Rorsman (Lund)

The President of the International Pigment Cell Society and Japanese Pigment Cell Society are permanently invited, ex officio, to the Steering Committee, together with J. Bagnara, editor of Pigment Cell Research.

MESSAGE FROM THE HON. SECRETARY, PATRICK RILEY

As the 1987 Annual Subscriptions are now due I would be grateful if Members will arrange for payment as soon as possible. Please make use of the form below. If you require a proforma invoice or have any other difficulties regarding methods of payment of your subscription please write directly to :

The Hon. Secretary
European Society for Pigment Cell Research
Department of Chemical Pathology
University College and Middlesex School of Medicine
Cleveland Street
London W1P 6DB
United Kingdom

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ESPCR Annual Subscription 1987

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ESPCR/S2

LETTER TO THE EDITOR OF



PIGMENT CELL BULLETIN

Sir,

The EORTC Melanoma Group Exchange Programme : a Multicentric Monoclonal Antibody Study

In the frame of the EORTC Malignant Melanoma Group, we undertook a large multicentric study on the specificity of a number of anti-melanoma monoclonal antibodies (Mabs) and on the reproducibility of immunohistological testing methods. As a final goal, the immunology subgroup has delineated a series of research objectives to be achieved during the next two years. First the group will come up with a panel of 25 or more Mabs to be used in immunohistopathology as an aid for a better discrimination between benign conditions like naevus and malignancy like melanoma, with a special emphasis on Mabs showing a preferential reactivity for "borderline" lesions. Second, a series of Mabs will be selected which are directed against membrane structures of which the expression or the absence of expression in primary malignant cells might be of prognostic value. Finally, the group will propose the most suitable Mabs to be used for imaging. In order to obtain a more accurate definition of the exact reactivity spectrum of each Mab under study, we developed, with the help of the EORTC Data Center, a standard form for the evaluation of the results. These forms are conceived in a way which should allow them to be analyzed in a computer programme. The present status of the Mabs Data Bank is more than 2.000 forms on 25 Mabs. Eleven institutions in Europe are currently collaborating. The preliminary results will be presented in Sorrento.

Yours sincerely,

S. CARREL
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CURRENT LITERATURE IN



We acknowledge the valuable assistance of
Ms Linda ALBRECHT and the financial support
of Lawrence M. Gelb Research Foundation.

PIGMENT CELL RESEARCH

During the year 1986, 93 publications on pigment cell research were found in computerized data banks (Medline and Chemical Abstracts). Four key subjects have been selected and 4 specialists from our Committee will briefly comment on them, separately, in the 4 issues of the Bulletin.

- 1) Melanin biology, biochemistry
- 2) Tyrosinase, enzyme; photobiology
- 3) Differentiation, hormones
- 4) Melanoma : this issue (F. Lejeune)

MELANOMA

Current literature on MELANOMA reviewed by F. Lejeune

In the data bank for 1986 up to September, 16 papers deal with melanoma as a pigment cell.

Carcinogenesis

(47)* Kanno et al, Acta Pathol Jpn 36:1-14, 1986, studied the histogenesis of the intradermal melanocytic tumours induced in BDF1 mice by topical DMBA and TPhorbol acetate. Only the melanocytes of the perifollicular melanocytic network (PFM) proliferated to form the tumours and not the epidermal nor the hair follicular melanocytes.

Biological properties

(36) Herlyn D. et al, Cancer Res 46:1339-1343, 1986 succeeded in transplanting human cutaneous naevi onto nude mice.

(77) Porro G. et al, Tumori 72:15-20, 1986, compared serum free synthetic medium with FCS. Three human melanoma cell lines were Ia positive and melanocytic in serum conditions, whereas

* : figures in brackets refer to the number in the data bank. The Editor can provide copies of the abstract if available.

without serum they became pigmented and lost the Ia antigen. They conclude that serum free medium promotes differentiation.

(39) Hoal-Van Helden E. et al, Br J Cancer 54:287-295, 1986, characterized 7 human melanoma cell lines according to melanogenesis and secretion of plasminogen activators.

(9) Berkelhammer J. et al, Cancer Res 46:2923-2928, 1986, point to the necessity of a rigorous methodology for limiting the occurrence of phenotypic instability of melanoma after propagation in vivo and in vitro.

Diagnosis and morphology

(32) Gomori J. et al, Radiology 158:443-335, 1986, report that NMR can produce images due to the paramagnetic effects of radicals present in melanin. They were able to distinguish between pigmented melanoma and other tissues except fat.

(18) Coderre J. et al, J Nucl Med 27:1157-1164, 1986, confirm that iodinated thiouracil can be incorporated into melanin and has therefore a potential use for diagnosis and therapy.

(70) Pavel S. et al, J Clin Chem Clin Biochem 24:167-173, 1986, using methan ionization of hexafluoroisopropyl and/or pentafluoropropionyl derivative of indolic compounds of the urine, were able to detect, in some cases, a decrease in the excretion of the eumelanin-related substances after chemotherapy.

(0) Ghanem G. et al, Eur J Cancer Clin Oncol 22:535-536, 1986, found that the alpha-MSH serum levels measured by specific RIA are increased in malignant melanoma and may fall in cases of response to chemotherapy.

(38) Hirano T., Acta Pathol Jpn 36:733-743, 1986, made an immunohistochemical study of 52 human melanomas using anti-S100 protein antibodies but did not use antimelanoma antibodies.

(75) Perry M. et al, Acta Cytol 30:385-396, 1986, describe the morphological analysis of 174 cases of malignant melanomas biopsied by fine needle aspiration. They found a majority of epitheloid cells in lymph node aspirates. In 60% of the cases, intracellular melanin was lacking, indicating that metastatic melanoma has a propensity to de-differentiate.

(48) Katenkamp D. et al, Zentralbl Allg Pathol 131:107-118, 1986, demonstrate a mediastinal melanocytic schwanoma which could easily be misinterpreted as melanoma.

(19) Cole E. et al, Arch Ophtalmol 104:98-101, 1986, report on a case where a cutaneous malignant melanoma had metastasized to the vitreous of the eye, a very rare clinical entity.

Therapy - Drugs

(40) Hu F. et al, Br J Dermatol 114:17-26, 1986, describe the effects of dicarboxylic acids (C9 and C12) on normal and malignant melanocytes in culture. Besides the fact that these compounds are competitive inhibitors of tyrosinase, they produce lesions in mitochondria.

(72) Pawelek J. et al, Cancer Res 46:493-497, 1986, report on the in vitro cytotoxicity of DOPA phosphate esters (position 3 and/or 4) on mouse melanoma. They found that these compounds are cytotoxic toward melanoma cells and that it can be enhanced 3 fold by MSH and prevented by phenylthiourea.

(85) Stephens T. et al, Int J Radiat Biol Relat Stud Phys Chem Med 49:169-175, 1986, found that the radiosensitivity of the B16 melanoma is not significantly influenced by melanin content.

MELANIN

Melanin biology and biochemistry

For this issue only, G. Prota has selected the references without comment owing to the short delay and the abundance of the material. Some abstracts are printed for their interest. Review of the subject will appear in further issues.

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Abstract : Interaction between Fe²⁺ ions and melanoproteid granules (MPG) of bovine eye pigment epithelium was studied by gamma-resonance spectroscopy. MPG was found to form complexes with bi- and three-valent ferrum ions. MPG can both directly bind Fe²⁺ ions and oxidize them Fe³⁺ inactive in prooxidant state and bind the latter. The activity of ferrum ion binding increases when suspension is illuminated with visible light and pH of the incubation solution increases. The protein part of MPG does not participate in the complex formation with ferrum ions. The complex formation proceeds mainly by carboxyl, amino- and imino-groups of melanin polymer.

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1986.

Abstract : The intragranular location of carboxyl groups was tinctorially determined in human substantia nigra neuromelanin granules, human inferior olive lipofuscin granules, and mouse meningeal melanosomes. Soluble and insoluble lipid was stained with beta naphthol Sudans in unoxidized and oxidized frozen and paraffin sections containing neuromelanin or lipofuscin. Nile blue demonstrated carboxyls in unoxidized neuromelanin, lipofuscin, and melanin, and in oxidized neuromelanin and lipofuscin. Carbodiimide demonstrated carboxyls in unoxidized and oxidized lipofuscin and oxidized neuromelanin. In all instances, staining for carboxyls was inhibited by prior mild methylation, and proof of their presence was obtained by a pre-staining, step-wise, alternating, and repetitive mild demethylation, mild methylation sequence. Structurally, carboxyls were demonstrated in the neuromelanin granule's soluble lipid-free lipofuscin component, in the meningeal melanosome's melanin component, and virtually throughout the lipofuscin granule. The following structural and chemical basis was proposed for the different resistance of Nile blue staining of melanosomes and of neuromelanin and lipofuscin to acetone extraction. Nile blue forms an insoluble complex with melanosomal dopa-melanin's quinonoid, diphenolic, and undissociated carboxyl units. Such complex formation does not occur in neuromelanin's carboxyl-free dopamine-melanin component, however. Instead, Nile blue ionogenically bonds with dissociated carboxyls belonging to the neuromelanin granule's lipofuscin component.

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- Berjian RA, Kanter PM, Bhakoo HS, Tan MH, Lawrence DD: Pre-treatment effects on the uptake/retention kinetics of L-dopa in Harding-Passey melanoma. *J Invest Dermatol* 86:560-562, 1986.

- Berkelhammer J, Luethans TN, Hook RR Jr, Oxenhandler RW: Phenotypic instability of mouse melanomas after propagation in vivo and in vitro. *Cancer Res* 46:2923-2928, 1986.

- Boulton M, Marshall J: Effects of increasing numbers of phagocytic inclusions on human retinal pigment epithelial cells in culture : a model for aging. *Br J Ophthalmol* 70:808-815, 1986.

- Bruenner U, Burnside B: Pigment granule migration in isolated cells of the teleost retinal pigment epithelium. *Invest Ophthalmol Vis Sci* 27:1634-1643, 1986.

- Burchill SA, Thody AJ, Ito S: Melanocyte-stimulating hormone, tyrosinase activity and the regulation of eumelanogenesis and pheomelanogenesis in the hair follicular melanocytes of the mouse. *J Endocrinol* 109:15-21, 1986.

Abstract : Skin tyrosinase levels and the eumelanin and pheomelanin contents of the hair were measured in pubertal and adult C3H-HeA*vy mice that grow dark and golden yellow hair respectively. Hair growth was initiated by plucking and the skin tyro-

sinase levels, which increased during the growth of new hair and peaked at around 9 days after plucking, were higher during the growth of dark hair in the pubertal mice than during the growth of yellow hair in the adult mice. Although there was only a twofold difference in the phaeomelanin contents of these two types of hair, the dark hair of the pubertal mice contained over 20 times more eumelanin than the golden-yellow hair of the adult mice. These results suggest that the changes in coat colour in C3H-HeA*vy mice are due mainly to changes in eumelanin synthesis by the hair follicular melanocytes and that the production of this pigment requires higher levels of the enzyme tyrosinase than does the production of phaeomelanin. These changes did not appear to be related to plasma alpha-MSH levels. Nevertheless, administration of alpha-MSH increased skin tyrosinase activity in the pubertal mice that were growing dark hair and produced a twofold increase in the eumelanin content of the hair. However, it had no such effects in adult mice and also failed to affect the phaeomelanin content of the hair in both groups of mice. In contrast to alpha-MSH, bromocriptine decreased skin tyrosinase levels and the eumelanin content and increased the phaeomelanin content of the hair in pubertal mice.

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- Chakraborty C, Hatta S, Ichihashi M, Mishima Y, Ueda M, Hayashibe K, Tsuji M, Mojamdar M: *Biol Role Proteinases Their Inhib Skin (Proc.Int.Symp)*, Ogawa H. et al (Eds), Elsevier, New York, pp. 217-225, 1986.

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Abstract : Thiouracil and various derivatives are selectively incorporated into the melanin pigment of melanomas during biosynthesis by serving as false melanin precursors. Using the transplantable Harding-Passey melanoma carried in BALB/c mice, we have extended our previous studies with sulfur-35 (³⁵S) thiouracil. The persistence of high levels of (³⁵S)thiouracil in tumor for periods of up to 2 wk has been demonstrated; during this time the drug content in normal tissues returned to near background levels. The variety of iodine isotopes available makes iodothiouracil a particularly promising melanoma-localizing agent. Tumor uptake and biodistribution of (³⁵S)thiouracil and iodothiouracil (both iodine-127 (¹²⁷I) and iodine 125 (¹²⁵I) labeled) have been compared and were found to be essentially the same. The selectivity of (¹²⁵I)thiouracil for melanoma has been qualitatively demonstrated by autoradiography of whole-body sections and quantitated by analysis of tumor and selected tissues. Iodothiouracil was also shown to localize in remote

secondary metastases using a metastatic variant of the Harding-Passey melanoma currently being developed in our laboratory. These studies confirm the melanoma localizing capabilities of an iodinated thiouracil, and therefore the potential of using iodinated thiouracil derivatives for diagnosis and therapy of melanotic melanomas.

- Conlee JW, Abdul-Baqi KJ, McCandless GA, Creel DJ: Differential susceptibility of noise-induced permanent threshold shift between albino and pigmented guinea pigs. *Hear Res* 23:81-91, 1986.

Abstract : Evidence that reduced levels of cochlear melanin are associated with increased auditory sensitivity, increased levels of auditory fatigue and an increased susceptibility to noise-induced hearing loss led us to investigate the effects of noise exposure on the cochlear microphonic (CM) in albino and pigmented English shorthair guinea pigs. CMs were recorded from the round window prior to and at 90 min and 7 days after exposure to 45 min of 126 dB noise. Threshold for the first detectable elicitation of the CM for four pure tones were determined and the output voltage of each cochlea was measured in 10 dB steps through intensity levels which produced a maximum voltage amplitude in the CM voltage rollover. This analysis demonstrated that : albino guinea pigs displayed significantly lower auditory thresholds than did pigmented animals before exposure to noise; thresholds were elevated to comparable levels in both groups 90 min after noise exposure; pigmented guinea pigs showed a reliable recovery in CM thresholds 7 days after exposure to noise while thresholds in the albinos remained elevated to the same degree at both 90 min and 7 days after noise; 90 min after noise exposure, the maximum voltage output of albino cochleas was significantly less than that recorded from the cochleas of the pigmented guinea pigs. These results demonstrate that albino guinea pigs are more susceptible to the ototoxic effects of high intensity noise than pigmented guinea pigs. Converging evidence indicates that some aspects of cochlear function involve melanin pigment and that its absence may produce auditory abnormalities. Reduced melanin pigmentation may also contribute to such phenomena as noise-induced threshold shifts and individual differences in noise-induced hearing loss.

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- Corradini MG, Napolitano A, Prota G: A biosynthetic approach to the structure of eumelanins. The isolation of oligomers from 5,6-dihydroxy-1-methylindole. *Tetrahedron* 42:2083-2088, 1986.

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1021, 1986.

- DeMattei M, Levi AC, Fariello RG: Neuromelanin pigment in substantia nigra neurons of rats and dogs. *Neurosci Lett* 72:37-42, 1986.

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Abstract : The effects of chronically administered 5 alpha-dihydrotestosterone and estradiol-17 beta on the dorsal costovertebral spots and scrotal skin of intact and hypophysectomized prepubertal male Syrian hamsters were analyzed morphometrically. The 5 alpha-dihydrotestosterone increased pigmentation (optical density) of costovertebral spots and scrotal skin without altering the percentage of pigmented area in intact animals. Spot size and pigment density also increased significantly in hypophysectomized hamsters, but here was no change in the percentage of pigmented area. The 5 alpha-dihydrotestosterone did not alter the percentage of pigmentation in any area of scrotal skin in hypophysectomized animals. In contrast, estradiol produced a dose-related decrease in the number of scrotal skin melanocytes in intact animals. The androgen-induced increase in pigmentation of costovertebral spot hair follicles was reversed by estradiol, which increased pigmentation around the sebaceous glands. These observations suggest that androgenic stimulation of pigmentation in male hamsters is direct, takes place prior to puberty, is probably tissue specific, and is antagonized by estrogens. The differential response to these steroids of melanocytes adjacent to hair follicles and around the perimeter of sebaceous glands may result from changes in the oxidation state of premelanin, an alteration in melanocyte size and shape, or an actual change in the rate of melanin synthesis.

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Abstract : Six freshly enucleated, unfixed human eyes with choroidal melanomas were imaged on a 1.4-T superconducting mag-

netic resonance (MR) imaging system. Immediately thereafter the eyes were sectioned, and tumor samples were removed for study on a variable-field (0.19-1.4 T) nuclear MR spectroscopy unit. Shorter T1 and T2 relaxation times were observed in those tumors with the greater concentrations of melanin. This is believed to result from the paramagnetic effect of radicals known to exist in melanin. High magnetic field MR imaging can enable one to distinguish between pigmented melanomas; proteinaceous effusions; fresh and subacute hematomas; and nonmelanotic melanoma to be distinguished from fat or amelanotic melanoma from other nonpigmented tumors.

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- Hu F, Mah K, Teramura DJ: Effects of dicarboxylic acids on normal and malignant melanocytes in culture. *Br J Dermatol* 114:17-26, 1986.

Abstract : We have shown that dicarboxylic acids (C9 and C12), known competitive inhibitors of tyrosinase, are selectively cytotoxic to malignant melanogenic melanocytes but not to normal pigmented cells or to amelanotic or non-melanogenic melanoma cells. The main target of this toxicity appears to be the mitochondria, which become markedly swollen and vacuolated. The mechanism of their action has been thought to be due to interference with oxidoreductases in the mitochondria. However, our results suggest that this cytotoxicity most probably does not result simply from inhibition of mitochondrial enzymes, but is closely related to the melanin biosynthesis pathway.

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- Abstract : Scavenging of superoxide radicals by melanin is a possible factor in the photoprotection afforded by melanin pigments. The reaction between superoxide anions and melanins has been studied by electron spin resonance and spin trapping methods. It was found that superoxide anions react to produce melanin free radicals in a reaction inhibited by superoxide dismutase but not by catalase. The rate of radical formation depends on the concentration of melanin and superoxide, the pH of the medium and the presence of diamagnetic metal ions. The melanin pigment competes with the enzyme superoxide dismutase for removal of superoxide radicals. It was found that the xanthine-xanthine oxidase system is not suitable for studying the reaction of superoxide with melanin, as the enzymatic activity of xanthine oxidase is considerably inhibited by melanin.
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Abstract : Melanin-pigments are found in various parts of the inner ear, especially in the neighbourhood of those epithelia that are believed to be involved in the secretion and/or absorption of endolymphatic fluid. Microprobe analysis (LAMMA, X-ray) measurements were performed in different parts of the inner ear in tissues containing melanin. The tissues were shock-frozen, freeze-dried and embedded in Earle's medium (Spurr). The semi-thin sections used for microprobe analysis were cut dry in a conventional ultramicrotome and mounted on copper grids. Experimental manipulation of the endolymph ionic composition (increased Na⁺) stimulated the migration of melanosomes from the perinuclear region into the dendritic processes and the rearrangement of the dendritic processes in a close vicinity of the presumably transporting epithelia. The intracellular ion measurements showed the affinity of divalent ions for melanin (Mg⁺⁺, Ca⁺⁺, Sr⁺⁺ and Ba⁺⁺). It is proposed that melanin represents a physiologically important "reservoir" for essential trace elements and by its binding/release may play a key role in the enzymatically controlled processes of ionic pumps.

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Abstract : We have shown that morpholine, a cyclic amine, exerts a selective inhibition of growth on melanocytic pigmented cell lines compared to nonpigmented cells. The ID₅₀ of morpholine for the pigmented B-16 cell line HFH was 1200 micrograms/ml, compared to values greater than 2400 micrograms/ml for baby hamster kidney, Chinese hamster ovary and NP, an unpigmented primate cell line. Two other cyclic amines piperazine and

piperidine, were similarly found to be selectively toxic to melanocytes. This selective toxicity could be synergistically enhanced by pretreatment of the cells with theophylline, a stimulator of tyrosinase activity, which indicates that the selective toxicity may be associated with melanin synthesis. Low passage HFH, high passage HFH and Syrian hamster melanoma RPMI 1846 cells that were pretreated with theophylline showed between 13 and 29% greater toxicity compared to controls treated with theophylline or morpholine alone. Unpigmented NP primate cells, Chinese hamster ovary and mouse fibroblast L929 remained unaffected. These cyclic amines join a list of other amines that have also been shown to be melanocytotoxic.

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Abstract : Most pigment cells during embryogenesis arise from the cranial or truncal portion of the neural crest and migrate to the skin, hair bulbs, choroid of the eye, the inner ear, leptomeninges, and other tissues. Cells of the retinal pigment epithelium come from a different source, namely, the primitive forebrain, and are involved in the formation of the retina and the optic nerves and tracts. Most pigment cells in all parts of the body seem to be constant in number and function until approximately middle age (the fourth or fifth decade of life). Thereafter, the number of melanocytes in the skin, hair, and eyes and the number of nevi begin to decrease. One function of pigment cells may be to eradicate oxygen radicals that are responsible in part for inducing malignancies and are also involved in the aging process. Possibly one result of the loss of melanocytes from the various organs is acceleration of the aging process in a permissive environment for the development of malignancies.

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tion (optical screening), but also by active chemical inhibition of the reaction. It is assumed that the observed active inhibition is due to the interaction between DOPA-melanin and the free radical products generated in cardiolipin upon UV illumination. It is concluded that the high photoresistance of melanin-containing cells of retinal pigment epithelium is due to the ability of melanosomes to exert strong inhibition of photo-induced lipid peroxidation.

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Abstract : We have isolated a pigment cell-specific cDNA clone from a B16 mouse melanoma cDNA library by differential hybridization. The mRNA of isolated cDNA is highly expressed in B16 melanoma cells and in black mouse (C57BL/6) skin, but is not detectable in mouse neuroblastoma cells nor in K1735 mouse amelanotic melanoma cells. The protein sequence deduced from the nucleotide sequence of the cloned cDNA shows significant similarity to the entire region of *Neurospora tyrosinase*. To know the identity of cDNA, we transfected K1735 amelanotic melanoma and COS-7 cells with the cDNA carried in a simian virus 40 vector (pKCRH2). We confirmed that the isolated cDNA encodes mouse tyrosinase by immunofluorescence staining of transfected cells using two different anti-T4-tyrosinase monoclonal antibodies. Tyrosinase is composed of 513 amino acids with a molecular weight of 57,872 excluding a hydrophobic signal peptide of 24 amino acids.

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Abstract : Spectral reflectance of the eye was assessed in four young Caucasian subjects with the Utrecht densitometer. Three retinal locations were studied, the fovea, the optic disk and a spot 12 deg temporal on the horizontal meridian. Reflectance

was measured with the visual pigments bleached away. The measuring field subtended 2,5 deg. The reflectance factor, relative to an artificial eye with a focal distance of 21.3 mm, was found to be lowest in the blue (0.1% for 419 nm) and highest in the red (10% for 711 nm). A model with six parameters, four densities of (non-photolabile) ocular pigments and two reflectance factors, was proposed to explain the experimental findings. A good fit to the data was obtained and the calculated densities of the ocular pigments came close to data found in the literature.

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ANNOUNCEMENTS



RELATED ACTIVITIES

Pigment Cell Journal

The pigment cell is a common thread that links many disciplines. Its cellular and developmental biology, function, and composition provide a common basis for studying phenomena as diverse as protection from predators, changes in body temperature, and skin cancers such as melanoma. Until now, no single journal has encompassed the broad spectrum of topics that have in common pigment cells as a target of investigation. A new journal, **Pigment Cell Research**, fills this gap by providing a forum for the exchange of information on basic and applied aspects of pigment cell biology.

The interdisciplinary nature of pigment cell research makes scientists dependent on new perspectives offered to one another through publication in a specialized forum. The bimonthly format of **Pigment Cell Research** assures prompt dissemination of information from the following subdisciplines of pigment cell biology :

- cell biology including ultrastructure, organellogenesis, intracellular movements, and melanogenesis
- developmental biology including determination, differentiation, transformation, and pattern formation
- pigment chemistry and biophysics
- melanoma including clinical, experimental, and comparative aspects
- biochemistry including enzymology and metabolism
- genetics including molecular biology, phenotypic expressions, and clinical and oncological aspects
- physiology including color change and functional aspects
- endocrinology including melanotropins and other hormones
- composition, function, and control of invertebrate pigment cells
- photobiology, basic and clinical aspects
- dermatology, especially hypo- and hyperpigmentation
- pigmentation and sexual characteristics
- immunological aspects of pigmentation

This new journal welcomes original articles reporting new theories and experimental results. In addition to high-quality original research papers, **Pigment Cell Research** will publish brief communications and invited mini-reviews. The journal's 8 1/4" x 11" format will allow for high-quality reproduction of micrographs. Future issues may include special communications, commentaries, and book reviews. All submissions will be carefully reviewed by a panel of internationally distinguished in-

investigators. Manuscripts for consideration should be submitted to : Dr Joseph Bagnara, Editor-in-Chief, College of Medicine, Dept of Anatomy, The University of Arizona, Tucson, Arizona 85724.

Pigment Cell Research will be of immense value to researchers and fellows in anatomy; biochemistry; biophysics; behavior; cellular, molecular, evolutionary, and developmental biology; chemistry; dermatology; ecology; endocrinology; neurology; genetics; immunology; internal medicine; vertebrate and invertebrate zoology; morphology; oncology; pharmacology; and physiology.

EORTC Malignant Melanoma Spring Meeting

We would like to invite you to our next group meeting :
April 24-24, 1987 in Strasbourg
c/o Prof. Dr. E. Grosshans / Dr Truchetet
Clinique Dermatologique
Place de l'Hôpital 1
F - 67091 Strasbourg
Phone : 88 36 71 11

If you are interested in participating, please write to :
Prof. Ulrich Kleeberg
H.O.P.A.
Max-Brauer-Allee 52
D - 2000 Hamburg
Phone : 40-380 21 20

WHO Melanoma Meeting - May 1987, Roma

The meeting will be held at the invitation of Prof. R. Cavaliere on Monday May 4 and Tuesday 5, 1987, at Hotel Forum - Via Tor de' Conti 25-30, 00184 Roma - Tel. (06) 6792446 - Telex : 622549.

The meeting will begin on Monday morning and will probably close after lunch on Tuesday.

If you are interested to be invited as an observer, please apply to N. Cascinelli, Director
W.H.O. Melanoma Programme
Istituto dei Tumori
Via Venezian 1
I - 20133 Milano

17th WORLD CONGRESS OF DERMATOLOGY - MAY 24-27, 1987, BERLIN

A number of sessions of interest to those working on basic and clinical aspects of pigmentation will be held.